23. A method according to claim 22 wherein said substance inhibits CYP2A6 and is methoxsalen, psoralen, tranylcypromine, pilocarpine, coumarin, chromone, esculetin, phenelzine, paroxetine, selegiline, or pargyline.

24. A kit in the use in the method of claim 22 or 23 comprising (a) nicotine and (b) one or more substances selected from the group consisting of (i) substances which inhibit CYP2A activity; (ii) substances which inhibit transcription, translation of the gene encoding CYP2A, or both; and (iii) substances which delete all or a portion of the gene encoding CYP2A.

REMARKS

Claims 1-34, as amended, appear in this application for the Examiner's review and consideration. Claims 22 and 23 have been amended to more particularly point out the claimed subject matter and to correct inadvertent minor spelling and editorial errors, but no new matter has been added. Applicants also submit a new declaration in compliance with 37 C.F.R. § 1.67(a) identifying the application by application number and filing date.

Claims 1-34 are subject to a restriction requirement. Applicants respectfully traverse.

The Office Action maintains the restriction requirement is proper because the kit of claim 24 can be used in a materially distinct process such as treating wounds. This statement, however, is merely conclusory and does not meet the *prima facie* requirement for demonstrating that either the claims are in a separate classification, separate status in the art, or a different field of search. MPEP 803 (8th Ed. 2001). In fact, claim 24 is classified within the same class and subclass as claims 22 and 23. This is important because where the claims of an application define the same essential characteristics of a *single* disclosed embodiment of an invention, restriction therebetween should never be required. MPEP 806.03. As claim 24 is dependent upon claim 22 or 23, the Office Action is hard pressed to suggest a separate utility.

Applicants respectfully remind the Examiner that every requirement to restrict has two aspects: (a) the reasons (as distinguished from the mere statement of conclusion) why the inventions *as claimed* are either independent or distinct; and (B) the reasons for insisting upon restriction therebetween. MPEP 808 (8th Ed. 2001). The particular reasons relied on by the Examiner for holding that inventions as claimed are independent or distinct should be concisely stated. A mere statement of conclusion is inadequate. MPEP 816 (8th Ed. 2001).

Accordingly, Applicants maintain that claim 24 should be examined with claims 22 and 23, *i.e.* Groups III and IV should be examined within the application.

Claims 22 and 23 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for the reasons set forth on pages 4 and 5 of the Office Action. Claims 22 and 23 have been amended, rendering this rejection moot.

Claim 22 is understandable by a skilled artisan following standard punctuation rules. For example, semicolons divide the subsections of part B, while the term "both" only applies to section (b)(ii). In other words, the phrase "or both" applies to "substances which inhibit transcription, translation of the gene encoding CYP2A activity." Claim 22, however, has been amended to clarify this reading. Claim 23 has been amended to recited the Markush group in proper format. *See*, MPEP 2173.05(h)(II) (8th Ed. 2001).

Thus, the rejection of claims 22 and 23 under 35 U.S.C. § 112, second paragraph, cannot stand and should be withdrawn.

Claims 22 and 23 stand rejected under 35 U.S.C. 103(a) as rendered obvious over U.S. patent No. 5,760,049 which issued to N. Viner on June 2, 1998 ("Viner") for the reasons set forth on pages 5 and 6 of the Office Action. Applicants respectfully traverse.

The consistent criterion for determination of obviousness is whether the prior art would have suggest to one of ordinary skill in the art that claimed subject matter should be carried out and would have a reasonable likelihood of success. *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). As the Examiner is well aware, in order to form a proper basis for a rejection under 35 U.S.C. § 103, the prior art must provide some suggestion, either explicit or implicit, of the combination that allegedly renders a claimed invention obvious. M.P.E.P., § 2142 (June 1998), *see also, Panduit Corp. v. Denisson Manufacturing Co.*, 1 U.S.P.Q.2d 1593, 1597 (Fed. Cir. 1987). The Examiner can satisfy the burden of showing obviousness of the combination only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. *In re Sang Su Lee*, 277 F.3d 1338, 1343, 61 U.S.P.Q.2d 1430 (Fed. Cir. 2002); citing *In re Fritch*, 972 F.2d 1260, 1265, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The need for specificity is paramount, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected the components for combination in the manner claimed. *Id.* The Examiner's conclusory statements do not adequately address the issue of motivation to combine; the factual question of motivation is

material to patentability, and can not be resolved on subjective belief and unknown authority. *Id.*

Viner discloses an oral drug composition comprising an effective amount of (1) an acetylcholine receptor antagonist and (2) an acetylcholine esterase reactivator as well as a method for controlling tobacco use and alleviating withdrawal symptoms due to the cessation of tobacco use (col. 2, ll. 42-47). A class of compounds used as acetylcholine esterase reactivators are oximes, generally defined by the formula $(R\text{-}CR{=}NOH)^{+}X^{-}$ (col. 3, ll. 7-9). In addition to the acetylcholine esterase reactivator and the acetylcholine receptor antagonist, it is within the scope of the present invention to co-administer additional compounds to assist in achieving the desired result or to provided additional cooperative treatment (col. 5, ll. 27-31).

The present claims are directed to methods for enhancing the effectiveness of nicotine replacement therapy comprising contemporaneously administering to an individual in need (a) nicotine and (b) one or more substances selected from the group consisting of (i) substances which inhibit CYP2A activity; (ii) substances which inhibit transcription, and/or translation of the gene encoding CYP2A activity; and (iii) substances which delete all or a portion of the gene encoding CYP2A.

The Office Action fails to establish a prima facie case of obviousness because neither Viner nor the Office Action provided any suggestion as to how the skilled artisan would obtain the present claims. Viner discloses the use of acetylcholine esterase reactivator and the acetylcholine receptor antagonist to control tobacco use. Although the reactivator and antagonist are directed to acetylcholine, neither are disclosed to be a CYP2A inhibitor. In fact, Viner is silent about CYP2A inhibitors. Viner focuses on acetylcholine, and makes no mention of the importance of mitigating the degradation of nicotine or reducing the production of procarcinogenic compounds, as disclosed in the present invention. More importantly, Viner fails to recognize that one of the important aspects in nicotine therapy replacement is to regulate the activity of human cytochrome P450 CYP2A. Accordingly, there is no objective teaching to obtain the present claims from Viner.

Furthermore, not only does Viner fail to disclose or suggest either implicitly or explicitly the present claims, Viner teaches against the present claims by disclosing an oral composition. As disclosed in the present invention, nicotine delivered in oral compositions is degraded by enzymes in the liver, thus, nicotine is systemically delivered at lower concentrations compared to delivery via inhalation. Mere oral administration decreases the effectiveness of any treatment if not administered with an enzyme inhibitor, *i.e.* a CYP2A

inhibitor administered substantially simultaneously or sequentially. As Viner fails to disclose the use of CYP2A inhibitor, Viner creates the problem the current invention seeks to solve. A skilled artisan in view of Viner is not aware of this shortcoming and consequently, will repeat the mistakes of the prior art, contrary to the present claims.

The only method by which a skilled artisan would obtain the present claims from Viner is by ignoring Viner's teachings and using the present claims as a blueprint. At a minimum, Viner requires two compounds an acetylcholine esterase reactivator and an acetylcholine receptor antagonist. Although additional compounds may be added, these two compounds are required. Without guidance or suggestion, the skilled artisan must ignore the use of acetylcholine esterase reactivator and acetylcholine receptor antagonist, and somehow include a CYP2A inhibitor within the composition. This outcome is only possible by using hindsight analysis by using the present claims as a blueprint, an unacceptable methodology to establish obviousness.

Accordingly, the rejection of claims 22 and 23 under 35 U.S.C. § 103(a) as rendered obvious by Viner cannot stand and should be withdrawn.

Accordingly, it is believed that claims 1-34 are now in condition for allowance, early notice of which would be appreciated.

If any outstanding issues remain, the examiner is invited to telephone the undersigned at the telephone number indicated below to discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees to Brobeck, Phleger & Harrison, LLP Deposit Account No. 50-1640.

Respectfully submitted,

Dated: 4/23/02

By: for Craig L. Puckett (Reg. No. 43,023) Reg No 27,399

Brobeck, Phleger & Harrison LLP
Intellectual Property Department
1333 H Street, N.W., Suite 800
Washington, D.C. 20005
(202) 220-6000

EXHIBIT A
MARKED VERSION OF THE CLAIMS
U.S. PATENT APPLICATION SERIAL NO. 09/584,669

22. (Amended) A method for enhancing the effectiveness of nicotine replacement therapy comprising contemporaneously administering to an individual in need (a) nicotine and (b) one or more substances selected from the group consisting of (i) substances which inhibit CYP2A activity; (ii) substances which inhibit transcription, and/or translation of the gene encoding CYP2A activity[, or both]; and (iii) substances which delete all or a portion of the gene encoding CYP2A.

23. (Amended) A method according to claim 22 wherein said substance inhibits CYP2A6 and is [selected from] methoxsalen, psoralen, tranylcypromine, pilocarpine, coumarin, chromone, esculetin, phenelzine, paroxetine, selegiline, or [and] pargyline.

24. (Amended) A kit in the use in the method of claim 22 or 23 comprising (a) nicotine and (b) one or more substances selected from the group consisting of (i) substances which inhibit CYP2A activity; (ii) substances which inhibit transcription, translation of the gene encoding CYP2A, or both; and (iii) substances which delete all or a portion of the gene encoding CYP2A.